642 **^{11}C-MET-PET for monitoring of early treatment response in multiple myeloma**

K. Lückerath[1], C. Lapa[1], S. Samnick[1], H. Einsele[2], S. Knop[2], A.K. Buck[1].
[1]Uniklinik Würzburg, Klinik und Poliklinik für Nuklearmedizin, Würzburg, Germany, [2]Uniklinik Würzburg, Medizinische Klinik II, Würzburg, Germany

Background: Multiple myeloma (MM) is a haematologic malignancy originating from clonal plasma cells. Although overall survival has improved over the last decade, MM essentially remains incurable. Several studies have demonstrated the usefulness of ^{18}F-FDG-PET for diagnosis, staging and prognostication. However, the role of functional imaging for therapeutic management of MM remains to be determined. More specific tracers addressing hallmarks of cancer, e.g. paraprotein biosynthesis, are needed. This study aimed at evaluating the usefulness of the amino acid tracer ^{11}C-MET and of ^{18}F-FDG to monitor treatment responses to anti-myeloma therapy and their potential to characterise tumour heterogeneity.
Materials and Methods: The influence of proteasome inhibition (Bortezomib, MLN9708, Carfilzomib) on radiotracer uptake of different MM cell lines and of patient-derived CD138^{+} plasma cells was analysed. Radiotracer uptake was related to tumour biology, e.g. to marker gene expression, paraprotein levels, growth rate and sensitivity towards treatment. Likewise, mice xenotransplanted with the MM cell line MM.1S were imaged with ^{11}C-MET and ^{18}F-FDG using μPET. Tumour-to-background ratios before and after 24 h treatment with Bortezomib were determined.
Results: Treatment with either proteasome inhibitor reduced ^{11}C-MET and ^{18}F-FDG uptake in MM cell lines; this was clearly more pronounced with ^{11}C-MET. Changes in tracer retention were accompanied by lower proliferation rates, intracellular Ig light chain levels and a switch from high to low CD138 expression. In xenotransplanted mice tumour retention of ^{11}C-MET at baseline exceeded that of ^{18}F-FDG 3-fold. Already 24 h after injection of Bortezomib ^{11}C-MET intensity decreased 2.5-fold in the treatment, but not control group. No difference between baseline intensity or control and treatment groups could be detected with ^{18}F-FDG. This finding could be confirmed in patient-derived MM cells.
Conclusion: Our results suggest that generally responses to anti-MM treatment can be monitored well with ^{11}C-MET and, limited, with ^{18}F-FDG. Monitoring of very early responses seems to be feasible with ^{11}C-MET only. These data support our previous notion of ^{11}C-MET being superior over routine functional imaging with ^{18}F-FDG. We plan to transfer our findings to a human pilot study to find out if ^{11}C-MET-PET allows accurate discrimination of responders and non-responders and if it impacts patient management. Concluding, ^{11}C-MET might serve as a biomarker for MM opening the possibility for individualised therapies and promptly adapted treatment strategies.
No conflict of interest.